## SEQUENCE LISTING

- <110> Saucier, Caroline Park, Morag Pawson, Anthony J. Lai, Ka-Man
- <120> SHC MODULATION AND USES THEREOF
- <130> MGU-0024
- <150> US 60/447,709
- <151> 2003-02-19
- <160> 16
- <170> PatentIn version 3.1
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Gly Val Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln 50 60

Ser Met Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu 65 70 75 80

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His His Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr 145 150 155 160

Ala Glu Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala 165 170 175

Cys His Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser 180 185 190

Thr Ile Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn 195 200 205

Pro Pro Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly 210 215 220

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Pro Val Gly Gly Asp Pro Glu Val Arg Lys Gln Met Pro Pro Pro 290 295 300

Pro Cys Pro Gly Arg Glu Leu Phe Asp Asp Pro Ser Tyr Val Asn Val 305 310 315 320

Gln Asn Leu Asp Lys Ala Arg Gln Ala Val Gly Gly Ala Gly Pro Pro 325 330 335

Asn Pro Ala Ile Asn Gly Ser Ala Pro Arg Asp Leu Phe Asp Met Lys 340 345 350

Pro Phe Glu Asp Ala Leu Arg Val Pro Pro Pro Pro Gln Ser Val Ser 355 360 365

Met Ala Glu Gln Leu Arg Gly Glu Pro Trp Phe His Gly Lys Leu Ser 370 375 380

Arg Arg Glu Ala Glu Ala Leu Leu Gln Leu Asn Gly Asp Phe Leu Val 385 390 395 400

Ser Gly Gln Pro Lys His Leu Leu Leu Val Asp Pro Glu Gly Val Val 420 425 430

Arg Thr Lys Asp His Arg Phe Glu Ser Val Ser His Leu Ile Ser Tyr 435 440 445

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Glu Leu Pro Ser Pro Ser Ala Ser Ser Leu Gly Pro Ile Leu Pro Pro 35 40 45

Leu Pro Gly Asp Asp Ser Pro Thr Thr Leu Cys Ser Phe Phe Pro Arg 50 55 60

Met Ser Asn Leu Arg Leu Ala Asn Pro Ala Gly Gly Arg Pro Gly Ser 65 70 75 80

Lys Gly Glu Pro Gly Arg Ala Ala Asp Asp Gly Glu Gly Ile Asp Gly
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Ala Ala Met Pro Glu Ser Gly Pro Leu Pro Leu Leu Gln Asp Met Asn 100 105 110

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Leu Gly Gly Glu Glu Trp Thr Arg His Gly Ser Phe Val Asn Lys Pro 130 135 140

Thr Arg Gly Trp Leu His Pro Asn Asp Lys Val Met Gly Pro Gly Val 145 150 155 160

Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln Ser Met 165 170 175

Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu Ala Ile 180 185 190

Ser Leu Val Cys Glu Ala Val Pro Gly Ala Lys Gly Ala Thr Arg Arg 195 200 205

Arg Lys Pro Cys Ser Arg Pro Leu Ser Ser Ile Leu Gly Arg Ser Asn 210 215 220

Leu Lys Phe Ala Gly Met Pro Ile Thr Leu Thr Val Ser Thr Ser Ser 225 230 235 240

Leu Asn Leu Met Ala Ala Asp Cys Lys Gln Ile Ile Ala Asn His His 245 250 255

Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr Ala Glu 260 265 270

Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala Cys His 275 280 285

Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser Thr Ile 290 295 300

Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn Pro Pro 305 310 315 320

Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly Ser Ala 325 330 335

Trp Asp Glu Glu Glu Glu Pro Pro Asp His Gln Tyr Tyr Asn Asp 340 345 350

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Arg Glu Gly Ala Ala Pro Gly Ala Ala Arg Pro Thr Ala Pro Asn Ala 370 375 380

Gln Thr Pro Ser His Leu Gly Ala Thr Leu Pro Val Gly Gln Pro Val 385 390 395 400

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Gln Pro Lys His Leu Leu Leu Val Asp Pro Glu Gly Val Val Arg Thr 530 535 540

Lys Asp His Arg Phe Glu Ser Val Ser His Leu Ile Ser Tyr His Met 545 . 550 555 560

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Glu Leu Pro Ser Pro Pro Ala Ser Ser Leu Gly Pro Ile Leu Pro Pro 35 40 45

Leu Pro Gly Asp Asp Ser Pro Thr Thr Leu Cys Ser Phe Phe Pro Arg

50 55 60

Met Ser Asn Leu Arg Leu Ala Asn Pro Ala Gly Gly Arg Pro Gly Ser Lys Gly Glu Pro Gly Arg Ala Ala Asp Asp Gly Glu Gly Ile Val Gly 85 Ala Ala Met Pro Asp Ser Gly Pro Leu Pro Leu Gln Asp Met Asn 100 105 Lys Leu Ser Gly Gly Gly Gly Arg Arg Thr Arg Val Glu Gly Gln Gln 115 120 Leu Gly Glu Glu Trp Thr Arg His Gly Ser Phe Val Asn Lys Pro 130 Thr Arg Gly Trp Leu His Pro Asn Asp Lys Val Met Gly Pro Gly Val Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln Ser Met Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu Ala Ile 180 Ser Leu Val Cys Glu Ala Val Pro Gly Ala Lys Gly Ala Thr Arg Arg 195 200 Arg Lys Pro Cys Ser Arg Pro Leu Ser Ser Ile Leu Gly Arg Ser Asn 210 215 Leu Lys Phe Ala Gly Met Pro Ile Thr Leu Thr Val Ser Thr Ser Ser 225 230 Leu Asn Leu Met Ala Ala Asp Cys Lys Gln Ile Ile Ala Asn His His Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr Ala Glu 260 Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala Cys His 275 280

Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser Thr Ile

290 295 300

Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn Pro Pro 310 315 Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly Ser Ala 325 330 Trp Asp Glu Glu Glu Glu Pro Pro Asp His Gln Tyr Tyr Asn Asp 340 345 Phe Pro Gly Lys Glu Pro Pro Leu Gly Gly Val Val Asp Met Arg Leu Arg Glu Gly Ala Ala Pro Gly Ala Ala Arg Pro Thr Ala Pro Asn Ala Gln Thr Pro Ser His Leu Gly Ala Thr Leu Pro Val Gly Gln Pro Val Gly Gly Asp Pro Glu Val Arg Lys Gln Met Pro Pro Pro Pro Cys 405 Pro Gly Arg Glu Leu Phe Asp Asp Pro Ser Tyr Val Asn Val Gln Asn 420 Leu Asp Lys Ala Arg Gln Ala Val Gly Gly Ala Gly Pro Pro Asn Pro 435 Ala Ile Asn Gly Ser Ala Pro Arg Asp Leu Phe Asp Met Lys Pro Phe 450 Glu Asp Ala Leu Arq Val Pro Pro Pro Pro Gln Ser Val Ser Met Ala 465 Glu Gln Leu Arg Gly Glu Pro Trp Phe His Gly Lys Leu Ser Arg Arg 485 Glu Ala Glu Ala Leu Leu Gln Leu Asn Gly Asp Phe Leu Val Arg Glu 500 Ser Thr Thr Thr Pro Gly Gln Tyr Val Leu Thr Gly Leu Gln Ser Gly 515 520 Gln Pro Lys His Leu Leu Val Asp Pro Glu Gly Val Val Arg Thr

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Lys Asp His Arg Phe Glu Ser Val Ser His Leu Ile Ser Tyr His Met 545 550 555 560

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<213> Mus musculus

<400> 8

Gly Gln Leu Gly Gly Glu Glu Trp Thr Arg His Gly Ser Phe Val Asn 20 25 30

Lys Pro Thr Arg Gly Trp Leu His Pro Asn Asp Lys Val Met Gly Pro  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Gly Val Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln
50 60

Ser Met Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu 65 70 75 80

Ala Ile Ser Leu Val Cys Glu Ala Val Pro Gly Ala Lys Gly Ala Thr 85 90 . 95

Arg Arg Lys Pro Cys Ser Arg Pro Leu Ser Ser Ile Leu Gly Arg
100 105 110

Ser Asn Leu Lys Phe Ala Gly Met Pro Ile Thr Leu Thr Val Ser Thr 115 120 125

Ser Ser Leu Asn Leu Met Ala Ala Asp Cys Lys Gln Ile Ile Ala Asn 130 135 140

His His Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr 145 150 155 160

Ala Glu Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala 165 170 175

Cys His Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser 180 185 190

Thr Ile Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn 195 200 . 205

Pro Pro Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly 210 215 220

Ser Ala Trp Asp Glu Glu Glu Glu Glu Pro Pro Asp His Gln Tyr Tyr 225 230 235 240

Asn Asp Phe Pro Gly Lys Glu Pro Pro Leu Gly Gly Val Val Asp Met 245 250 255

Arg Leu Arg Glu Gly Ala Ala Arg Pro Thr Leu Pro Ser Ala Gln Met 260 265 270

Ser Ser His Leu Gly Ala Thr Leu Pro Ile Gly Gln His Ala Ala Gly 275 280 285

Asp His Glu Val Arg Lys Gln Met Leu Pro Pro Pro Pro Cys Pro Gly 290 295 300 .

Arg Glu Leu Phe Asp Asp Pro Ser 305 310

Tyr Val Asn Ile Gln Asn Leu Asp 315 320

Lys Ala Arg Gln Ala Gly Gly Gly Ala Gly Pro Pro Asn Pro Ser Leu 325 330 335

Asn Gly Ser Ala Pro Arg Asp Leu Phe Asp Met Lys Pro Phe Glu Asp 340 345 350

Ala Leu Arg Val Pro Pro Pro Gln Ser Met Ser Met Ala Glu Gln 355 360 365

Leu Gln Gly Glu Pro Trp Phe His Gly Lys Leu Ser Arg Arg Glu Ala. 370 375 380

Glu Ala Leu Leu Gln Leu Asn Gly Asp Phe Leu Val Arg Glu Ser Thr 385 390 395 400

Thr Thr Pro Gly Gln Tyr Val Leu Thr Gly Leu Gln Ser Gly Gln Pro 405 410 415

Lys His Leu Leu Val Asp Pro Glu Gly Val Val Arg Thr Lys Asp 420 425 430

His Arg Phe Glu Ser Val Ser His Leu Ile Ser Tyr His Met Asp Asn 435 440 445

His Leu Pro Ile Ile Ser Ala Gly Ser Glu Leu Cys Leu Gln Gln Pro 450 455 460

Val Asp Arg Lys Val

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<211> 1739

<212> DNA

<213> Mus musculus

<400> 9

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tccctgggac ccattctgcc tcctctgccg ggggacgata gtccgactac cctgtgttcc 180

ttctttcccc ggatgagcaa cctgaagctg gccaatcctg ctggggggg cctggggcct 240 aaaggggagc caggaaaggc tgctgaagat ggggaaggga gtgcaggggc agcccttcgg gactcaggcc tcttgcccct cctccaggac atgaacaagc tgagtggagg cggcgggcgc 360 aggactcggg tagaaggggg ccagctgggg ggcgaggagt ggaccagaca cgggagcttt 420 gtcaataagc ccacacgagg ctggctgcat cccaacgaca aagtcatggg acctggggtt 480 tectaettgg tteggtaeat gggetgtgtg gaggtettae agteaatgeg ageeettgae ttcaataccc ggactcaggt caccagggag gccatcagtt tggtgtgtga agctgtgcct ggtgccaaag gggcgacaag gaggagaaag ccttgtagcc gcccactcag ctccatcctg gggaggagta acctgaagtt tgctggaatg ccaatcactc tcactgtgtc taccagcagc cttaacctca tggcagccga ctgcaaacag atcattgcca accatcacat gcaatctatc 780 tetttegegt eeggtgggga teeggacaea getgagtatg ttgeetatgt tgeeaaagae cctgtgaatc agagagcctg ccatatcctg gagtgtcctg aagggcttgc tcaggatgtc 900 atcagcacca togggoaggo otttgagttg ogottcaaac agtatotcag gaatccaccg aagctggtca ccccccatga caggatggct ggctttgatg gctcagcttg ggatgaggag 1020 gaagaagagc cccctgacca tcagtactac aatgactttc cagggaagga accccctctt ggtggggtgg tagatatgag gcttcgggaa ggggctgctc gacccactct gcctagtgcc 1140 cagatgtcca gccacttggg agctacactg cctatagggc agcatgctgc aggagaccat gaagteegta aacagatgtt geeteegeeg eettgeeeag geagagaaet ettegatgae 1260 ccctcctatg tcaacatcca gaatctagac aaggcccggc aggctggggg tggggctggg cccccaaatc cttctcttaa tggcagtgca ccccgagacc tttttgacat gaagcccttt 1380

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<212> PRT

<213> Mus musculus

<400> 10

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Glu Leu Pro Ser Pro Ser Ala Ser Ser Leu Gly Pro Ile Leu Pro Pro 35 40 45

Leu Pro Gly Asp Asp Ser Pro Thr Thr Leu Cys Ser Phe Phe Pro Arg 50 55 60

Met Ser Asn Leu Lys Leu Ala Asn Pro Ala Gly Gly Arg Leu Gly Pro 65 70 75 80

Lys Gly Glu Pro Gly Lys Ala Ala Glu Asp Gly Glu Gly Ser Ala Gly 85 90 95

Ala Ala Leu Arg Asp Ser Gly Leu Leu Pro Leu Leu Gln Asp Met Asn 100 105 110

Lys Leu Ser Gly Gly Gly Arg Arg Thr Arg Val Glu Gly Gln
115 120 125

Leu Gly Gly Glu Glu Trp Thr Arg His Gly Ser Phe Val Asn Lys Pro 130 135 140 Thr Arg Gly Trp Leu His Pro Asn Asp Lys Val Met Gly Pro Gly Val 145 150 155 160

4 1 4

Ser Tyr Leu Val Arg Tyr Met Gly Cys Val Glu Val Leu Gln Ser Met 165 170 175

Arg Ala Leu Asp Phe Asn Thr Arg Thr Gln Val Thr Arg Glu Ala Ile 180 185 190

Ser Leu Val Cys Glu Ala Val Pro Gly Ala Lys Gly Ala Thr Arg Arg 195 200 205

Arg Lys Pro Cys Ser Arg Pro Leu Ser Ser Ile Leu Gly Arg Ser Asn 210 215 220

Leu Lys Phe Ala Gly Met Pro Ile Thr Leu Thr Val Ser Thr Ser Ser 225 230 235 240

Leu Asn Leu Met Ala Ala Asp Cys Lys Gln Ile Ile Ala Asn His His 245 250 255

Met Gln Ser Ile Ser Phe Ala Ser Gly Gly Asp Pro Asp Thr Ala Glu 260 265 270

Tyr Val Ala Tyr Val Ala Lys Asp Pro Val Asn Gln Arg Ala Cys His 275 280 285

Ile Leu Glu Cys Pro Glu Gly Leu Ala Gln Asp Val Ile Ser Thr Ile 290 295 300

Gly Gln Ala Phe Glu Leu Arg Phe Lys Gln Tyr Leu Arg Asn Pro Pro 305 310 315 320

Lys Leu Val Thr Pro His Asp Arg Met Ala Gly Phe Asp Gly Ser Ala 325 330 335

Trp Asp Glu Glu Glu Glu Pro Pro Asp His Gln Tyr Tyr Asn Asp 340 345 350

Phe Pro Gly Lys Glu Pro Pro Leu Gly Gly Val Val Asp Met Arg Leu 355 360 365

Arg Glu Gly Ala Ala Arg Pro Thr Leu Pro Ser Ala Gln Met Ser Ser 370 380

His Leu Gly Ala Thr Leu Pro Ile Gly Gln His Ala Ala Gly Asp His 385 390 395 400

Glu Val Arg Lys Gln Met Leu Pro Pro Pro Pro Cys Pro Gly Arg Glu 405 410 415

Leu Phe Asp Asp Pro Ser Tyr Val Asn Ile Gln Asn Leu Asp Lys Ala
420 425 430

Arg Gln Ala Gly Gly Gly Ala Gly Pro Pro Asn Pro Ser Leu Asn Gly
435
440
445

Ser Ala Pro Arg Asp Leu Phe Asp Met Lys Pro Phe Glu Asp Ala Leu 450 455 460

Arg Val Pro Pro Pro Gln Ser Met Ser Met Ala Glu Gln Leu Gln 465 470 475 480

Gly Glu Pro Trp Phe His Gly Lys Leu Ser Arg Arg Glu Ala Glu Ala 485 490 495

Leu Leu Gln Leu Asn Gly Asp Phe Leu Val Arg Glu Ser Thr Thr Thr 500 505 510

Pro Gly Gln Tyr Val Leu Thr Gly Leu Gln Ser Gly Gln Pro Lys His 515 520 525

Leu Leu Leu Val Asp Pro Glu Gly Val Val Arg Thr Lys Asp His Arg 530 535 540

Phe Glu Ser Val Ser His Leu Ile Ser Tyr His Met Asp Asn His Leu 545 550 555 560

Pro Ile Ile Ser Ala Gly Ser Glu Leu Cys Leu Gln Gln Pro Val Asp 565 570 575

Arg Lys Val

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1 5 10

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-<211> 9

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<223> RTK variants

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Asn Ala Thr Phe Val Asn Val Lys Cys 1  $\phantom{\bigg|}$